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ECHO

Antiretroviral drugs confuse universal antenatal blood screens

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All women infected with HIV should have their haemoglobin A_2 (HbA_2) concentrations recorded before they start antiretroviral drug treatment to avoid later suspicion antenatally of heterozygous β thalassaemia trait and unnecessary genetic counselling and analysis, say some UK doctors. In their experience HbA_2 concentration can be raised solely by the treatment.

This is likely to become more of a problem now that universal antenatal screening for blood disorders is to be introduced to areas of the UK where β thalassaemia is prevalent and because more and more fertile women are being treated with antiretroviral drugs for HIV infection. A benchmark HbA_2 value will allow doctors to judge whether to exclude heterozygous β thalassaemia.

The doctors reported on two cases in which pregnant women being treated with antiretroviral drugs had raised HbA_2 concentrations which were not associated with hypochromic, microcytic red cell indices characteristic of heterozygous β thalassaemia. One was in a 35 year old with asymptomatic HIV infection and hepatitis C infection since 1990, receiving antiretroviral drugs since 1992. Stavudine, didanosine, and nevirapine were changed to zidovudine, lamivudine, and efavirenz in 2000 and efavirenz to nelfinavir later, when she was eight weeks pregnant, to avoid teratogenic effects. Hb concentration was 124 g/l, HbA 95.7%, and HbA_2 4.3% on booking in to the antenatal clinic. This led to her and her partner's referral to counsellors—as if she were positive for heterozygous β thalassaemia—and testing of her partner, who was HIV positive but taking no antiretroviral drugs: Hb was 118 g/l, HbA 87.2%, and HbA_2 6.3%. Genetic analysis on her partner and to ascertain her carrier status for β thalassaemia and risk to the fetus showed that he had heterozygous β thalassaemia; sequencing showed no mutation in her β globlin gene. Healthy twins were born at term with normal results for full blood counts and on neonatal haemoglobinopathy screening.

The other case was in a 32 year old whose haemoglobin concentration was 90 g/l, HbA_2 1.6% in 1996 but who later contracted AIDS and in 1999 started receiving antiretroviral drugs. In early 2000 she was taking zidovudine, lamivudine, and nelfinavir; zidovudine was later replaced by stavudine because of severe anaemia. Later in 2000, when she was pregnant, blood tests at booking in disclosed an HbA_2 concentration of 3.9%, even though she had stopped zidovudine 10 weeks before. After counselling, blood tests confirmed that her partner did not have β thalassaemia. Two years later nelfinavir was changed to nevirapine to ensure compliance, and three months afterwards, during her second pregnancy, HbA_2 concentration was 2.9%.

Zidovudine has been reported to raise HbA_2 concentrations, and it seemed to do so in case 1. A similar effect may have been prolonged in case 2 because of the long half life of erythrocytes—120 days. HbA_2 concentration was normal two years later, without zidovudine, though stopping nelfinavir cannot be excluded as an alternative explanation for this.

Heterozygous β thalassaemia, which raises HbA_2 concentrations to 4–6%, is important in antenatal screening for blood disorders and shows hypochromic, microcytic red cell indices, but is not to be confused with other conditions with raised HbA_2 concentrations, like hyperthyroidism and megaloblastic anaemia or being HIV positive and taking antiretroviral drugs, when these markers are absent. Previous, selective antenatal screening of HbA_2 has been applied only when the characteristic markers of β thalassaemia are present or suspect. However, as these cases show, raised HbA_2 concentration on universal screening would not necessarily indicate β thalassaemia.

▲ Howard J, *et al. Journal of Clinical Pathology* 2005;**58**:556–558.